NIH Center for Scientific Review

peer review notes

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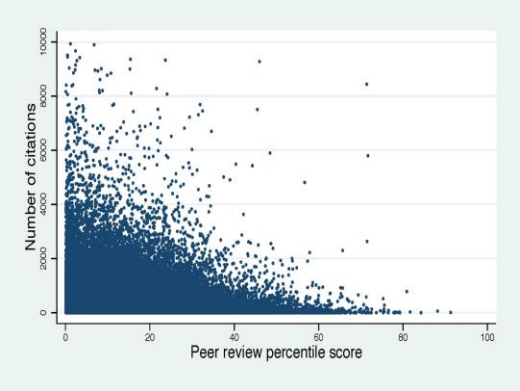
In this Issue

Peer Review Scores Correlated with Better Research Outcomes



Researchers from Harvard and Boston Universities recently cast a positive light on NIH reviewers. They published an article in Science magazine that helps address a key question: "Big names or big ideas: Do peer-review panels select the best science proposals?"

"We find that better-review scores are consistently associated with better research outcomes," said Dr. Danielle Li and Dr. Leila Agha from Harvard and Boston Universities respectively, "and that this relationship persists even when we include detailed controls for an investigator's publication history, grant history, institutional affiliations, career stage, and degree types."

Li and Agha examined over 130,000 R01 NIH grants awarded between 1980 and 2008, and tracked related publications, citations and patents. CSR made it possible for them to compare these factors with review scores while ensuring the confidentiality of this information.

"The most encouraging result is that they found there is something special about the highest-rated applications," said CSR Director Dr. Richard Nakamura, "reviewers are able to discern value beyond what one could from publications and citations."

Li and Agha showed that one–standard deviation worse score was associated with 15% fewer citations, 7% fewer publications, 19% fewer high-impact publications, and 14% fewer follow-on patents.

Noting that the data are noisy, Nakamura said, "We need to continue working with the scientific community to study and refine peer review."

"In the meantime," he added, "it's clear that a lot of great science gets left behind on the cutting room floor. But the main reason for this is the current low level of support."

Update on the Waves of Applications

"Reviewers and NIH staff can breathe a little easier," said CSR Director Dr. Richard Nakamura. "The waves of applications haven't increased after the initial surge we experienced following NIH's decision to remove limits on resubmissions." He noted that, after the policy change last April, incoming applications surged 15 percent. "In the last review cycle, the numbers stabilized, and now they appear to be resuming the slight decline we observed before the policy change."

He noted the numbers of incoming applications are still near historic highs, and to meet the new and projected demand, CSR has recruited 10 additional Scientific Review Officers and, of course, called on more scientists to review.

Policy Summary

Following an unsuccessful resubmission (A1) application, investigators may now submit the same idea as a new (A0) application for the next appropriate due date. Although a new (A0) application does not allow an introduction or responses to the previous reviews, the NIH encourages investigators to refine and strengthen all application submissions.

NIH's policy on overlapping applications remains in force: NIH will not accept an application that is similar to one that has been reviewed before the summary statement from the review of the earlier application has been released.

NIH Calls for More Grantees to Review

"When we ran the numbers, we discovered many NIH grantees haven't been doing their part," said CSR Director Dr. Richard Nakamura. "So NIH put out a call to remind them of their professional obligation to the community and encourage them to say yes when asked to serve on a peer review or advisory group."

To make sure more grantees heard the call, Nakamura joined with NIH's Deputy Director for Extramural Research Dr. Sally Rockey to post a joint notice on the popular Rock Talk Blog.

They acknowledged the difficulties NIH grantees face. "We know that pay lines are low and that your professional obligations are high, both of which made it more difficult to say yes when we ask," they said. "However, we believe that the professional obligation to serve as a peer reviewer is extremely important to keep this great enterprise going, particularly for those of you who currently have NIH support."

What the Data Reveal

Nakamura and Rockey summed up the situation: "NIH examined the peer review service records of scientists with current research project grant support and who have received a total of $1 million or more in total costs from NIH in the last 5 years. There are more than 25,500 scientists in this pool, and of these, 83% have participated in at least one peer review meeting in 5 years.

Looking closer at the data, if one meeting of peer review service per year would be considered a reasonable expectation for service, then currently fewer than half of these funded scientists (45%) achieved that level of service. It is important to note that not all funded investigators are asked to serve each year, and those individuals are also included in this figure.

In addition, there is an increase in service with more funded R01 grants. The data revealed that 42% of investigators with one R01 served at least one time per year, 59% of those with two R01s served at least one time per year, and 72% of those with three or more R01s served at least one time per year."

PIs with at Least $1M in NIH Funding in the Last Five Years

The following tables show the percentage of researchers who have received $1 million in NIH funding in the last five years and who have served on NIH peer review panels. Though HHMI, IOM and NAS researchers participate on peer review panels at lower levels, their overall support of the NIH extramural program is higher when you add their participation in other NIH advisory groups.

Participation in at least one NIH peer review meeting per year for five years	**Percentage**
All Funded PIs	45%
HHMI Members	36%
IOM Members	33%
NAS Members	21%

Participated in at least one NIH peer review *or advisory* meeting per year for five years	**Percentage**
All Funded PIs	48%
HHMI Members	47%
IOM Members	51%
NAS Members	34%

New CSR Efforts to Recruit Reviewers

A New Tool to Recruit Reviewers: The recent data run led CSR to develop lists of grantees who haven't served. We now give these lists to our Scientific Review Officers, and many of them used the lists to recruit new reviewers for this review round.

A New Way to Volunteer: CSR overhauled its Become a Reviewer Web page and established a new mechanism for researchers to volunteer. If you are not sure what study section would be the best fit, we encourage you to send your CV to csrvolunteer@mail.nih.gov, and we'll work to find a review group that may need your expertise.

Join the Conversation on the Rock Talk Blog

CSR Director Responds to Community Concerns

"In our many interactions with researchers each week, we hear your concerns and learn about your burdens," he said. "The truth is we usually share your concerns and have explored your suggestions."

"Our recent blog on 'Supporting the Call to Peer Review Service' led a number of reviewers and others to post suggestions, which in turn led me to comment on the most frequent suggestions."

- **Prescreen applications to reduce reviewer and applicant burdens.** NIH officials continue to discuss the challenges and possibilities of implementing new practices that could reduce reviewer and applicant burdens.

- **Restore coffee and refreshments at review meetings.** As the Department of Health and Human Services reads previous executive orders, NIH cannot do this. However, we continue to tell senior leaders how counter-productive this policy is to our collective goal of being efficient and productive.

- **Drop the new biosketch format.** NIH will monitor the new format to see if it lives up to its promise. It grew out of a concern that the earlier format tended to lead reviewers to judge applicants by looking at their publications and calculating journal impact factors rather than looking at the accomplishments themselves. The new format was designed to give applicants more credit for relevant accomplishments and to raise the level of review discussion.

- **Increase reviewer honorariums or lengthen their grants.** Reviewers have never gotten paid what their time is worth, but the scientific community has benefited greatly from the peer review process. Nonetheless, I'd like to see reviewers receive higher honorariums. But given our current budget, raising reviewer honorariums would mean cutting funding for grants or the infrastructure that supports them.

- **Change the reimbursement policy so travel costs don't go on IRS 1099s.** In earlier years, reviewers had to save and submit meal and misc. travel receipts to CSR. This effort was notoriously time consuming for reviewers and our staff. We started giving reviewers a flat amount to cover their per diem and misc. travel expenses after we saw how well this worked for the National Science Foundation. We were all dismayed to later learn these payments had to be reported to the IRS as income. The only way to change things would be for Congress to come together and change the tax law.

What Can CSR Do to Make Life Easier for Reviewers?

- Allow more reviewers who cannot attend a specific review meeting to do so by facilitating more hybrid -- face-to-face and video -- meetings.

- Host more peer review meetings in different cities so reviewers don't always have to travel to Washington, DC. We now host many meeting on the west coast, and we've recently added New Orleans and St. Louis and will add more cities in the future.

- Allow chartered reviewers and others with significant service to submit at any time applications that would otherwise be due on standard due dates.

- Offer chartered reviewers flexible service terms.

If you can think of other ways we could address these issues and do a better job, please join the conversation on the Rock Talk Blog.

Peer Review and Grant Reforms in Canada

Bold changes are underway in Canada, where the Canadian Institutes of Health Research (CIHR) is overhauling its grants and peer review systems. Dr. Jane Aubin CIHR's Chief Scientific Officer and Vice-President of Research, Knowledge Translation and Ethics came to CSR to discuss CIHR efforts at a recent CSR Director's Seminar.

"CIHR has been doing one of the more interesting peer review experiments," said CSR Director Dr. Richard Nakamura. "We thought now would be an interesting time to get an update, learn what has driven their changes, and discover how Canadian researchers have responded to them."

CIHR and NIH Face Similar Challenges

CIHR has a $1 Billion (Canadian) annual budget, which supports about 3,000 unique principal investigators and a total of 14,000 researchers. About 70% of its grants support investigator-initiated research. Though it is much smaller than NIH, both organizations face similar challenges: constricted budgets, low success rates, and overburdened applicants and reviewers. Both CIHR and NIH would like to do more to increase their abilities to identify and fund the most promising and innovative research.

CIHR Reforms

Guided by surveys and pilots, CIHR is implementing the following changes to meet these challenges and to address what it sees as a growing discrepancy between the evolution of research and the structure of its review committees and to address the need for greater peer review efficiencies:

- ***Simplify CIHR's investigator-initiated grant mechanisms by reducing them from 12 to 2:*** a "Foundation Scheme" is designed to support promising researchers at different career stages, and a "Project Scheme" is designed to advance promising research ideas.

- ***Have structured review criteria and bulleted critiques:*** Like NIH, CIHR has aligned the structure of its applications to its review criteria.

- ***Shift peer review from a committee-focused effort to an application-focused effort:*** CIHR assigns five online reviewers who are closely matched to each application, and they review the application via an Internet Assisted Review meeting. All applications submitted for a given scheme are reviewed in the same 2-3 day review period.

- ***Use multi*-stage reviews and shorter stage 1 applications to reduce applicant and reviewer burdens and increase efficiencies:** After online reviews, only the most highly ranked (green zone) and top gray-area (the next most highly ranked but where reviewer opinions are more variable) applications move forward. In the final stage, CIHR convenes face-to-face review meetings where applications are discussed only as needed.

- ***Rank applications instead of scoring them:*** Since reviewers can find it difficult to spread scores, CIHR has turned to ranking. Based on the analysis of data from pilots, it believes a ranking approach will prove to be a more useful measure for establishing a prioritized funding list.

What Do Canadian Researchers Think?

Aubin described the results of CIHR's surveys and how stakeholder input is guiding the reforms. The overall response has been positive, though more established grantees and reviewers have been more critical than others.

What Does CSR Think?

There was a lively discussion after her presentation, as our SROs questioned Aubin.

After the seminar, Nakamura discussed CSR's perspective. "As we look to the future, we still consider face-to-face reviews the gold standard for NIH reviews," he said. "However, we look forward to seeing how CIHR evaluates the success and effectiveness of their reforms and to learning things that could help us plot our own course."

Judge for Yourself: View the archived video presentation.

The Invention of Expansion Microscopy, a Diaper Compound, and the Power of Peer Review

Scientists can't break the laws of physics. This was a problem Dr. Edward Boyden faced at the Massachusetts Institute of Technology. The best light microscopes cannot bring key molecular structures into focus without losing track of the larger cellular context. But if scientists could see more deeply across a broader expanse of tissue—with nanoscale precision—they could potentially learn more about the abnormal biochemistry of disease, and come up with new targets for drug design.

With a positive assessment by CSR reviewers and a subsequent NIH Director's Pioneer Award for "high risk, high reward" research, a team led by Dr. Boyden turned this tough problem on its head, inventing expansion microscopy, a new approach to visualizing biological samples. The creativity and problem-solving potential of the strategy already has drawn the attention of scientists who investigate a variety of diseases, including neurodegenerative disorders and cancer.

"We found a way to magnify samples directly, rather than just trying to use a lens to magnify light from a sample," said Dr. Boyden, Associate Professor of Biological Engineering and Brain and Cognitive Sciences, at the MIT Media Lab and the MIT McGovern Institute. "It is turning out to really be useful."

To expand tissue samples and cells without altering their shapes, Dr. Boyden and graduate students Fei Chen and Paul Tillberg use a chemical polymer known for decades and popular as an absorbent in diapers.

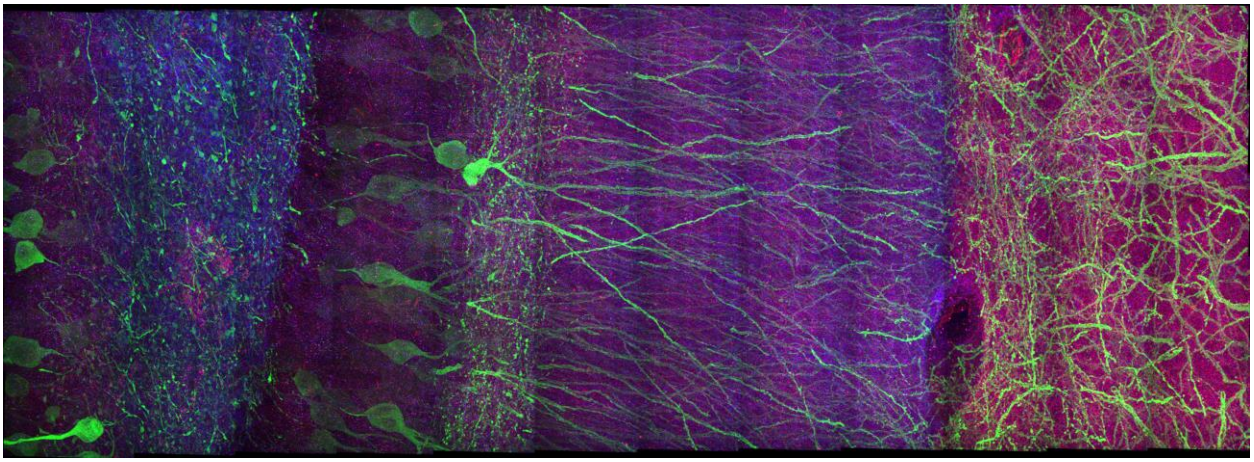
To enlarge a sample the scientists first tag the proteins within with fluorescent antibodies, and then embed the sample in an expandable polymer gel, made of polyacrylate. The polyacrylate binds to the fluorescent tags, and remains bound even after the protein is dissolved away. Adding water causes the polyacrylate to swell, as it does in a wet diaper, enlarging the entire fluorescently labeled sample without distortion.

Dr. Boyden's goal is to probe what's going on at a molecular level within signaling pathways inside neurons, without losing sight of the bigger picture that reveals what's happening within a larger network of nerve circuitry. So far, his research team has investigated expansion microscopy in lab-cultured brain cells and in slices of nerve tissue from mice.

"We have had a fantastic response from the neuroscience community, but the response from the cancer community also has been significant," said Dr. Boyden. "We now are engaged in collaborations to do cancer research, and the work also has generated interest in exploring how immune cells are arranged within organs in cancer and in autoimmune disease. That was a direct output from this high-risk, high-reward funding."

Dr. Boyden has a track record generating big ideas leading to major research success. A decade ago, he wanted to control and explore nerve signaling in living cells under the microscope on millisecond time scales. To accomplish this, as a Stanford University graduate student working on a side collaboration with Dr. Karl Deisseroth, now the D.H. Chen Professor of Bioengineering and of Psychiatry and Behavioral Sciences, he co-invented optogenetics, a technique in which researchers use light-sensitive, ion-channel proteins to convert light into electricity.

Dr. Boyden's continued success as a scientist who is skilled in developing new ways to record electrical activity from neurons and in devising other molecular techniques for learning more about what goes on in cells helped sway the scientists who reviewed his Pioneer Award proposal, noted Dr. Kip Ludwig, Program Director for Neural Engineering at the National Institute for Neurological Diseases and Stroke, which funds Dr. Boyden's Pioneer Award.



Expansion Microscopy of mouse brain tissue: Volume rendering of a portion of hippocampus showing neurons (expressing YFP, shown in green) and synapses [marked with anti-Bassoon (blue) and antibody to Homer1 (red)]

"The idea of the Pioneer Award and certain other NIH high-risk, high-reward grant mechanisms is to support big and bold ideas from researchers with a history of turning big and bold ideas into success stories," said Dr. Ludwig. "There are disadvantages to requiring all the smallest details at the application stage. With big ideas applied to big problems, science does not always go the way you expect it to, and the focus needs to be on the impact of the idea and the proven ability of the investigator to solve problems as they arise."

The results to date are exciting, but not exactly what Dr. Boyden initially proposed. "I wrote my Pioneer Award proposal partly on neural recording in three dimensions, but I also mentioned that I would love to do super-resolution imaging of brain circuits," he said.

Peer review of Pioneer Award proposals includes an interview and presentation before an audience of scientists. By the time of his presentation, Dr. Boyden's lab team had acquired early data on expansion microscopy. "I showed them an image of one of the very first cells we had expanded, and we proceeded to talk about this new technology that was not part of the original written proposal," said Dr. Boyden. To his relief, the reviewers endorsed moving the groundbreaking research forward.

While he continues to work on other big ideas, he expects his lab's success in expansion microscopy to become, dare we say — more expansive. "We are looking for polymers that expand bigger, that preserve structures even better, and that are even more compatible with biomolecules," he said.

"Our role is to build technology, and technology development doesn't always fit within hypothesis-driven or disease-focused paradigms. We often simply set out to build tools that are going to help people solve a whole bunch of problems."

— Jeffrey Norris

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